

### **REMARKS**

This application is a national stage filing of PCT/JP2004/004083. Claims 1-4 were present at the time of filing. In response to an initial Office Action, claims 2 and 4 were cancelled and new claims 5-7 were presented. Claims 1, 3 and 5-7 are currently pending in the application.

Claims 3 and 7 are amended above to clarify that the anti-adiponectin antibody used in the claimed latex reagent/method binds to native adiponectin. Support for the term “quantitatively” is found at page 1 of the specification, first paragraph. Additional support for the amendment is implicit in the description of a method to quantitatively and accurately measure adiponectin levels by detecting naturally-occurring adiponectin present in biological samples without first treating the sample to denature any native adiponectin or diluting the sample.

### ***Rejection Under 35 U.S.C. § 103***

The claims are rejected under 35 U.S.C. § 103(a) as being unpatentable over Sawai *et al.* in view of Arita *et al.* because, according to the Office Action, it would have been obvious to use the adiponectin specific polyclonal antibody of Arita *et al.* in the latex assay of Sawai *et al.*

Arita *et al.* discloses the development of an enzyme-linked immunosorbent assay (ELISA) to determine the levels of adiponectin in patient samples. The two-antibody “sandwich” assay disclosed in Arita *et al.* employs a monoclonal anti-adiponectin antibody as the capture antibody and a polyclonal anti-adiponectin antibody as the detection antibody; both antibodies were generated to recombinant adiponectin as antigen (p. 80, column 1, 10-12).

Arita *et al.* discovered that when using the particular combination of antibodies, both of which had been shown by Western blotting to recognize recombinant adiponectin (page 81, column 1, 1<sup>st</sup> full ¶ under RESULTS), the amount of native adiponectin detected in the plasma samples was lower than expected (page 81, column 2.) In order to get an accurate determination, it was necessary to boil the sample with SDS prior to assay to obtain a monomeric form of

adiponectin. Arita et al. does not teach or suggest that their polyclonal adiponectin antibody binds native adiponectin.

The present claims are amended above to clarify that the polyclonal anti-adiponectin antibody used in Applicants' claimed assay binds native adiponectin. There is likely to be some level of native adiponectin in any biological sample, and since the anti-adiponectin antibody of Arita et al. fails to detect it, an accurate assessment of the amount of adiponectin in a sample using the anti-adiponectin antibody of Arita et al. can only be obtained by pretreatment of the sample.

Applicants suggest that Arita *et al.* demonstrates, in general, that use of antibodies does not always produce the expected result and in particular, that the combination of monoclonal and polyclonal (recombinant) adiponectin-specific antibodies did not accurately detect native adiponectin in plasma samples without first treating the sample to denature the adiponectin. Despite their significant value as research tools, the successful use of antibodies in any context is unpredictable and generally, empirically determined. Applicants maintain that one of skill in the art would not have concluded or had an expectation, based on the teachings of Arita et al., that the polyclonal antibody disclosed therein was able to bind native adiponectin.

Accordingly, withdrawal of the rejection under 35 U.S.C. § 103(a) is respectfully requested.

It is respectfully submitted that the above-identified application is now in condition for allowance and favorable reconsideration and prompt allowance of these claims are respectfully requested. Should the Examiner believe that anything further is desirable in order to place the application in better condition for allowance, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted,

A handwritten signature in cursive script, reading "Kathy Smith Dias", written over a horizontal line.

Kathy Smith Dias  
Attorney for Applicants  
Reg. No. 41,707

Dated: May 7, 2009  
HESLIN ROTHENBERG FARLEY & MESITI P.C.  
5 Columbia Circle  
Albany, New York 12203  
Telephone: (518) 452-5600  
Facsimile: (518) 452-5579